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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/885,297	06/19/2001	Lonnie O'Neal Ingram	49950-59776	2679
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EDWARDS & ANGELL, LLP			EXAMINER	
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BOSTON, MA 02205			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 02/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application N .</b>	<b>Applicant(s)</b>
	09/885,297	INGRAM ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Manjunath N. Rao, Ph.D.	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 30 November 2004.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 44-49,51-53 and 55-59 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 44-49,51-53 and 55-59 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|   | 6) <input type="checkbox"/> Other: _____.                                   |

### **DETAILED ACTION**

Claims 44-49, 51-53, 55-59, are currently pending and are present for examination.

Applicants' amendments and arguments filed on 11-30-04, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically Examiner has withdrawn previous rejections of claims 97-99, 101-102 and 104 in view of claim cancellation by the applicants.

However in response to the indication of claims 44-49, 51-53, 55-59 as allowable applicants have now re-defined the phrase "derived from *Erwinia*" in much broader terms (see page 8 of Remarks) as opposed to the Examiner's conclusion (based on earlier response from the applicant) that the phrase specifically meant isolated from *Erwinia* only and not from any other source. In view of such re-definition Examiner has no other option except to re-institute the earlier rejections.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44, and claims 45-49, 51-53, 55-59, all of which depend from claim 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 44 recites the phrase "derived from *Erwinia*". The metes and bounds of this phrase is not clear to the Examiner. Literally, while the term "derived" means "to isolate from or obtain from a source",

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the above term could also mean “to arrive at by reasoning i.e., to deduce or infer” or also mean “to produce or obtain from another substance”. Therefore, it is not clear to the Examiner either from the specification or from the claims as to what applicants mean by the above phrase. It is not clear to the Examiner whether the endoglucanases encoded by *celZ* and *celY* encompasses specific endoglucanases encoded by polynucleotides of *Erwinia* as in “isolated from *Erwinia*” or whether it encompasses recombinants, variants and mutants of any endoglucanase of any other source and labeled as “derived from *Erwinia*”. As applicants have not provided a clear and specific definition for the above phrase, Examiner has interpreted the claims broadly to mean, that *celZ* and *celY* “derived from *Erwinia*” encompasses nucleic acid sequences which are recombinants, variants, or mutants encoding any endoglucanase from any source. A perusal of literature in the art indicates that there are other endoglucanases isolated from other bacterial or fungal sources with similar nomenclature and hence this phrase is all the more important in the context of the above claim.

Claim 44 and claims 45-49, 51-53, 55-59, all of which depend from claim 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 44 recites the phrase “additional enzymes”. First of all the metes and bounds of the above phrase is not clear to the Examiner. Furthermore, it is not clear to the Examiner whether the enzyme is added along with the host cell or whether applicants mean that the host cell “expresses an additional enzyme”. For both above reasons the claim is unclear to the Examiner.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 44-49, 51-53, 55-59, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant host cell suitable for degrading oligosaccharide or reducing the viscosity comprising, a first heterologous polynucleotide encoding a first endoglucanase under the transcriptional control of a surrogate promoter and, a second heterologous polynucleotide encoding a first endoglucanase under the transcriptional control of a surrogate promoter and an additional ethanologenic enzyme such as an pyruvate decarboxylase or alcohol dehydrogenase, wherein the first and second endoglucanase are expressed so that their activities are present in a ratio such that the degrading of said oligosaccharide is synergized and wherein the said first endoglucanase is encoded by *celZ* (or EGZ) and second endoglucanase is encoded by *celY* (or EGY), both of which are isolated from *Erwinia chrysanthemi*, wherein said host cells are bacterial cells such as *E.coli* or *Klebsiella oxytoca* and wherein the additional enzyme comprises enzymes such as β-glucosidase, exoglucanase, endoglucanase, pyruvate decarboxylase or alcohol dehydrogenase or a secretory enzyme which is either a *pul* or *out* gene product, does not reasonably provide enablement for a such a recombinant host cell comprising the polynucleotides encoding any two endoglucanases from any source as the first and the second endoglucanases under the control of any promoter from any source and such recombinant cells further comprising any additional enzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 44-49, 51-53, 55-59, are so broad as to encompass a recombinant host cell comprising the polynucleotides encoding any two endoglucanases from any source as the first and the second endoglucanases under the control of any promoter isolated from any source and such recombinant cells further comprising any additional enzymes. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA sequences that are broadly encompassed by the claims.

The applicants propose to use the above host cells comprising the above polynucleotides (specifically comprising polynucleotides of *E.chrysanthemi* encoding endoglucanases) which they demonstrate to exhibit synergy between each other for the production of ethanol. It appears that invention is solely based on the above phenomenon that inventors have observed with respect to the polynucleotides and the promoters isolated from *E.chrysanthemi*. Since it appears that the nucleotide sequence of *E.chrysanthemi* alone determines this type of synergy between each other, use of recombinant cells transformed with any polynucleotide encoding endoglucanase isolated from any or all sources including variants and mutants of *Erwinia* polynucleotides as proposed by the applicants may not lead to desired synergy in the host cells. This is because applicants have not shown that using any two polynucleotides

encoding any two endoglucanase from any source including variants and mutants and recombinants of *Erwinia* exhibits such synergistic effects. However, in this case the disclosure is limited to the host cells transformed with naturally occurring endoglucanase encoding polynucleotides isolated from *E.chrysanthemi*.

While recombinant and mutagenesis techniques are known and it is routine in the art to screen for multiple substitutions or modifications of nucleotides as encompassed by the instant claims, the base changes within a nucleic acid's sequence that can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given DNA to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass host cells transformed with any polynucleotides encoding endoglucanases because the specification does not establish: (A) that synergistic reactions occur between any two endoglucanases isolated from any source,( including mutants, variants and recombinants of *Erwinia*), under the control of any two promoters from any source; (B)regions of the any endoglucanase including that of *Erwinia* and its promoter DNA sequence which may be modified to obtain the above mentioned activity/utility; (C) the general tolerance of any endoglucanase encoding DNA or the any promoter DNA sequence to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any endoglucanase polynucleotide with an expectation of obtaining the desired biological function and utility; and (E) the specification provides

insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly host cells transformed with any endoglucanase encoding DNA fragment isolated from any source. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of DNAs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 44-49, 51-53, 55-59, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to recombinant cells comprising a genus of heterologous DNA encoding endoglucanases (including their promoters) which exhibit synergy.

The specification does not contain any disclosure of the structure of all DNA sequences encoding endoglucanase (including their respective promoters) which exhibit synergy. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of having many different structures. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The

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specification discloses only a single species (i.e., host cells transformed with *celY* and *celZ* of *E.chrysanthemi*) of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at [www.uspto.gov](http://www.uspto.gov).

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 44-49, 51-53, 55-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Liebl et al. (Microbiology, 1996, Vol. 142(9) :2533-2542) or Riedel et al. (Mol. Microbiol., 1998, Vol. 28(4):767-775). This rejection is based upon the public availability of a printed publication. Claims 44-49, 51-53, 55-59 of the instant application are drawn to a recombinant host cell suitable for degrading an oligosaccharide comprising a first heterologous polynucleotide segment encoding a first endoglucanase and a second heterologous polynucleotide segment encoding a second endoglucanase, wherein the polynucleotide segments are under the transcriptional control of a surrogate promoter and further comprises a

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polynucleotide segment expressing an additional enzyme such as an ethanologenic enzyme, wherein the host cell is a bacterial cell belonging to enterobacteriaceae family, *E.coli* and wherein the first and second endoglucanase is encoded by *celZ* (EGZ) and *celY* (EGY) *derived from Erwinia* and the two endoglucanases work in synergy with each other.

Liebl et al. disclose an identical host cell, *E.coli* which comprises two endoglucanases CelA and CelB working in synergy under the control of a surrogate promoter and which are capable of degrading a oligosaccharide/polysaccharide and further inherently express an additional enzyme such as an ethanologenic enzyme such as alcohol dehydrogenase. Examiner takes the position that CelA and CelB of the reference encompasses the claimed endoglucanases encoded by *celY* or *celZ* "derived from Erwinia" based on the broad interpretation of the phrase.

Riedel et al. also disclose an identical host cell, *E.coli* which comprises two endoglucanases CelY and CelZ capable of acting in synergy under the control of a surrogate promoter and which are capable of degrading a oligosaccharide/polysaccharide and further inherently express an additional enzyme such as an ethanologenic enzyme such as alcohol dehydrogenase. Examiner takes the position that CelY and CelZ of the reference encompasses the claimed endoglucanases encoded by *celY* or *celZ* "derived from Erwinia" based on the broad interpretation of the phrase. Therefore, Liebl et al. or Riedel et al. anticipate claims 44-49, 51-53, 55-59 as written.

Since all the above rejections were previously presented, Examiner has made this Office action as Final.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

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Manjunath N. Rao

January 27, 2005